

SEQUENCE LISTING

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<120> METALLOPROTEASE ACTIVATION OF MYOSTATIN, AND METHODS OF MODULATING
 MYOSTATIN ACTIVITY

<130> JHU1800-3

<150> US 60/486,863
 <151> 2003-07-10

<150> US 60/439,164
 <151> 2003-01-09

<150> US 60/411,133
 <151> 2002-09-16

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Lys Thr Val Leu Gln Asn Trp Leu Lys Gln Pro Glu Ser Asn Leu Gly
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 Met His Phe Thr Gln Val Leu Ile Ser Leu Ser Val Leu Ile Ala Cys
 1 5 10 15

ggt cca gtg ggt tat gga gat ata acg gcg cac cag cag cct tcc aca
 Gly Pro Val Gly Tyr Gly Asp Ile Thr Ala His Gln Gln Pro Ser Thr

48

96

20	25	30	
gcc acg gag gaa agc gag ctg tgt tcc aca tgt gag ttc aga caa cac Ala Thr Glu Glu Ser Glu Leu Cys Ser Thr Cys Glu Phe Arg Gln His 35	40	45	144
agc aag ctg atg aga ctg cat gcc atc aag tcc caa att ctt agc aaa Ser Lys Leu Met Arg Leu His Ala Ile Lys Ser Gln Ile Leu Ser Lys 50	55	60	192
ctc cga ctc aag cag gct cca aac atc agc cggt gtc aag cag Leu Arg Leu Lys Gln Ala Pro Asn Ile Ser Arg Asp Val Val Lys Gln 65	70	75	240
ctg tta ccc aaa gca ccg cct ttg caa caa ctt ctg gat cag tac gat Leu Leu Pro Lys Ala Pro Pro Leu Gln Gln Leu Leu Asp Gln Tyr Asp 85	90	95	288
gtt tta gga gat gac agt aag gat gga gct gtg gaa gag gac gat gaa Val Leu Gly Asp Asp Ser Lys Asp Gly Ala Val Glu Glu Asp Asp Glu 100	105	110	336
cat gcc acc aca gag acc atc atg acc atg gcc aca gaa cct gac ccc His Ala Thr Thr Glu Thr Ile Met Thr Met Ala Thr Glu Pro Asp Pro 115	120	125	384
att gtt caa gta gat cgg aaa ccg aag tgt tgc ttt ttc tcc ttc agt Ile Val Gln Val Asp Arg Lys Pro Lys Cys Cys Phe Phe Ser Phe Ser 130	135	140	432
ccg aag atc caa gcg aac ccg atc gta aga gcg cag ctc tgg gtt cat Pro Lys Ile Gln Ala Asn Arg Ile Val Arg Ala Gln Leu Trp Val His 145	150	155	480
ctg aga ccg gcg gag gag gcg acc acc gtc ttc tta cag ata tct ccg Leu Arg Pro Ala Glu Glu Ala Thr Thr Val Phe Leu Gln Ile Ser Arg 165	170	175	528
ctg atg ccc gtt aag gac gga gga aga cac cga ata cga tcc ctg aaa Leu Met Pro Val Lys Asp Gly Gly Arg His Arg Ile Arg Ser Leu Lys 180	185	190	576
atc gac gtg aac gca gga gtc acg tct tgg cag agt ata gac gta aag Ile Asp Val Asn Ala Gly Val Thr Ser Trp Gln Ser Ile Asp Val Lys 195	200	205	624
cag gtg ctc acg gtg tgg tta aaa caa ccg gag acc aac cga ggc atc Gln Val Leu Thr Val Trp Leu Lys Gln Pro Glu Thr Asn Arg Gly Ile 210	215	220	672
gag att aac gca tat gac gcg aag gga aac gac ttg gcc gtc act tca Glu Ile Asn Ala Tyr Asp Ala Lys Gly Asn Asp Leu Ala Val Thr Ser 225	230	235	720
acc gag act ggg gag gat gga ctg ctc ccc ttt atg gag gtg aaa ata Thr Glu Thr Gly Glu Asp Gly Leu Leu Pro Phe Met Glu Val Lys Ile 245	250	255	768
tca gag ggc cca aaa cga atc ccg agg gac tcc gga ctg gac tgc gat Ser Glu Gly Pro Lys Arg Ile Arg Arg Asp Ser Gly Leu Asp Cys Asp 260	265	270	816

gag aat tcc tca gag tct cgc tgc agg tac cct ctc act gtg gac Glu Asn Ser Ser Glu Ser Arg Cys Cys Arg Tyr Pro Leu Thr Val Asp 275 280 285	864
ttc gag gac ttt ggc tgg gac tgg att att gct cca aaa cgc tat aag Phe Glu Asp Phe Gly Trp Asp Trp Ile Ile Ala Pro Lys Arg Tyr Lys 290 295 300	912
gcg aat tac tgt tca gga gaa tgc gac tac atg tac ctg cag aag tat Ala Asn Tyr Cys Ser Gly Glu Cys Asp Tyr Met Tyr Leu Gln Lys Tyr 305 310 315 320	960
ccc cac acc cat ctg gtg aac aag gcc agt ccg aga gga acg gct ggg Pro His Thr His Leu Val Asn Lys Ala Ser Pro Arg Gly Thr Ala Gly 325 330 335	1008
ccc tgc tgc act ccc acc aag atg tct ccc atc aac atg ctt tac ttt Pro Cys Cys Thr Pro Thr Lys Met Ser Pro Ile Asn Met Leu Tyr Phe 340 345 350	1056
aac ggc aaa gag cag atc atc tac ggc aag atc cct tcg atg gta gta Asn Gly Lys Glu Gln Ile Ile Tyr Gly Lys Ile Pro Ser Met Val Val 355 360 365	1104
gac cgc tgt ggc tgc tca tga Asp Arg Cys Gly Cys Ser 370	1125
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Met His Phe Thr Gln Val Leu Ile Ser Leu Ser Val Leu Ile Ala Cys 1 5 10 15	
Gly Pro Val Gly Tyr Gly Asp Ile Thr Ala His Gln Gln Pro Ser Thr 20 25 30	
Ala Thr Glu Glu Ser Glu Leu Cys Ser Thr Cys Glu Phe Arg Gln His 35 40 45	
Ser Lys Leu Met Arg Leu His Ala Ile Lys Ser Gln Ile Leu Ser Lys 50 55 60	
Leu Arg Leu Lys Gln Ala Pro Asn Ile Ser Arg Asp Val Val Lys Gln 65 70 75 80	
Leu Leu Pro Lys Ala Pro Pro Leu Gln Gln Leu Leu Asp Gln Tyr Asp 85 90 95	

Val Leu Gly Asp Asp Ser Lys Asp Gly Ala Val Glu Glu Asp Asp Glu
 100 105 110

His Ala Thr Thr Glu Thr Ile Met Thr Met Ala Thr Glu Pro Asp Pro
 115 120 125

Ile Val Gln Val Asp Arg Lys Pro Lys Cys Cys Phe Phe Ser Phe Ser
 130 135 140

Pro Lys Ile Gln Ala Asn Arg Ile Val Arg Ala Gln Leu Trp Val His
 145 150 155 160

Leu Arg Pro Ala Glu Glu Ala Thr Thr Val Phe Leu Gln Ile Ser Arg
 165 170 175

Leu Met Pro Val Lys Asp Gly Gly Arg His Arg Ile Arg Ser Leu Lys
 180 185 190

Ile Asp Val Asn Ala Gly Val Thr Ser Trp Gln Ser Ile Asp Val Lys
 195 200 205

Gln Val Leu Thr Val Trp Leu Lys Gln Pro Glu Thr Asn Arg Gly Ile
 210 215 220

Glu Ile Asn Ala Tyr Asp Ala Lys Gly Asn Asp Leu Ala Val Thr Ser
 225 230 235 240

Thr Glu Thr Gly Glu Asp Gly Leu Leu Pro Phe Met Glu Val Lys Ile
 245 250 255

Ser Glu Gly Pro Lys Arg Ile Arg Arg Asp Ser Gly Leu Asp Cys Asp
 260 265 270

Glu Asn Ser Ser Glu Ser Arg Cys Cys Arg Tyr Pro Leu Thr Val Asp
 275 280 285

Phe Glu Asp Phe Gly Trp Asp Trp Ile Ile Ala Pro Lys Arg Tyr Lys
 290 295 300

Ala Asn Tyr Cys Ser Gly Glu Cys Asp Tyr Met Tyr Leu Gln Lys Tyr
 305 310 315 320

Pro His Thr His Leu Val Asn Lys Ala Ser Pro Arg Gly Thr Ala Gly
 325 330 335

Pro Cys Cys Thr Pro Thr Lys Met Ser Pro Ile Asn Met Leu Tyr Phe

340

345

350

Asn Gly Lys Glu Gln Ile Ile Tyr Gly Lys Ile Pro Ser Met Val Val
355 360 365

Asp Arg Cys Gly Cys Ser
370

<210> 9
<211> 50
<212> PRT
<213> Homo sapiens

<400> 9

Lys Asp Val Ile Arg Gln Leu Leu Pro Lys Ala Pro Pro Leu Arg Glu
1 5 10 15

Leu Ile Asp Gln Tyr Asp Val Gln Arg Asp Asp Ser Ser Asp Gly Ser
20 25 30

Leu Glu Asp Asp Asp Tyr His Ala Thr Thr Glu Thr Ile Ile Thr Met
35 40 45

Pro Thr
50

<210> 10
<211> 50
<212> PRT
<213> Artificial sequence

<220>
<223> Mutant peptide portion of human myostatin

<400> 10

Lys Asp Val Ile Arg Gln Leu Leu Pro Lys Ala Pro Pro Leu Arg Glu
1 5 10 15

Leu Ile Asp Gln Tyr Asp Val Gln Gln Asp Asp Ser Ser Asp Gly Ser
20 25 30

Leu Glu Asp Asp Asp Tyr His Ala Thr Thr Glu Thr Ile Ile Thr Met
35 40 45

Pro Thr
50

<210> 11

<211> 50
<212> PRT
<213> Artificial sequence

<220>
<223> Mutant peptide portion of human myostatin

<400> 11

Lys	Asp	Val	Ile	Arg	Gln	Leu	Leu	Pro	Lys	Ala	Pro	Pro	Leu	Arg	Glu	
1									5					10		15

Leu	Ile	Asp	Gln	Tyr	Asp	Val	Gln	Arg	Ala	Asp	Ser	Ser	Asp	Gly	Ser	
														20	25	30

Leu	Glu	Asp	Asp	Asp	Tyr	His	Ala	Thr	Thr	Glu	Thr	Ile	Ile	Thr	Met	
														35	40	45

Pro Thr
50

<210> 12
<211> 40
<212> PRT
<213> Homo sapiens

<400> 12

Gln	Leu	Leu	Pro	Lys	Ala	Pro	Pro	Leu	Arg	Glu	Leu	Ile	Asp	Gln	Tyr	
1									5					10		15

Asp	Val	Gln	Arg	Asp	Asp	Ser	Ser	Asp	Gly	Ser	Leu	Glu	Asp	Asp	Asp
													20	25	30

Tyr	His	Ala	Thr	Thr	Glu	Thr	Ile	
							35	40

<210> 13
<211> 40
<212> PRT
<213> Artificial sequence

<220>
<223> Mutant peptide portion of human myostatin

<400> 13

Gln	Leu	Leu	Pro	Lys	Ala	Pro	Pro	Leu	Arg	Glu	Leu	Ile	Asp	Gln	Tyr	
1									5					10		15

Asp	Val	Gln	Gln	Asp	Asp	Ser	Ser	Asp	Gly	Ser	Leu	Glu	Asp	Asp	Asp
													20	25	30

Tyr His Ala Thr Thr Glu Thr Ile
35 40

<210> 14
<211> 40
<212> PRT
<213> Artificial sequence

<220>
<223> Mutant peptide portion of human myostatin

<400> 14

Gln Leu Leu Pro Lys Ala Pro Pro Leu Arg Glu Leu Ile Asp Gln Tyr
1 5 10 15

Asp Val Gln Arg Ala Asp Ser Ser Asp Gly Ser Leu Glu Asp Asp Asp
20 25 30

Tyr His Ala Thr Thr Glu Thr Ile
35 40

<210> 15
<211> 30
<212> PRT
<213> Homo sapiens

<400> 15

Ala Pro Pro Leu Arg Glu Leu Ile Asp Gln Tyr Asp Val Gln Arg Asp
1 5 10 15

Asp Ser Ser Asp Gly Ser Leu Glu Asp Asp Asp Tyr His Ala
20 25 30

<210> 16
<211> 30
<212> PRT
<213> Artificial sequence

<220>
<223> Mutant peptide portion of human myostatin

<400> 16

Ala Pro Pro Leu Arg Glu Leu Ile Asp Gln Tyr Asp Val Gln Gln Asp
1 5 10 15

Asp Ser Ser Asp Gly Ser Leu Glu Asp Asp Asp Tyr His Ala
20 25 30

<210> 17

<211> 30
<212> PRT
<213> Artificial sequence

<220>
<223> Mutant peptide portion of human myostatin

<400> 17

Ala Pro Pro Leu Arg Glu Leu Ile Asp Gln Tyr Asp Val Gln Arg Ala
1 5 10 15

Asp Ser Ser Asp Gly Ser Leu Glu Asp Asp Asp Tyr His Ala
20 25 30

<210> 18
<211> 20
<212> PRT
<213> Homo sapiens

<400> 18

Glu Leu Ile Asp Gln Tyr Asp Val Gln Arg Asp Asp Ser Ser Asp Gly
1 5 10 15

Ser Leu Glu Asp
20

<210> 19
<211> 20
<212> PRT
<213> Artificial sequence

<220>
<223> Mutant peptide portion of human myostatin

<400> 19

Glu Leu Ile Asp Gln Tyr Asp Val Gln Asp Asp Ser Ser Asp Gly
1 5 10 15

Ser Leu Glu Asp
20

<210> 20
<211> 20
<212> PRT
<213> Artificial sequence

<220>
<223> Mutant peptide portion of human myostatin

<400> 20

Glu Leu Ile Asp Gln Tyr Asp Val Gln Arg Ala Asp Ser Ser Asp Gly

1

5

10

15

Ser Leu Glu Asp
20

<210> 21
<211> 10
<212> PRT
<213> Homo sapiens

<400> 21

Tyr Asp Val Gln Arg Asp Asp Ser Ser Asp
1 5 10

<210> 22
<211> 10
<212> PRT
<213> Artificial sequence

<220>
<223> Mutant peptide portion of human myostatin

<400> 22

Tyr Asp Val Gln Gln Asp Asp Ser Ser Asp
1 5 10

<210> 23
<211> 10
<212> PRT
<213> Artificial sequence

<220>
<223> Mutant peptide portion of human myostatin

<400> 23

Tyr Asp Val Gln Arg Ala Asp Ser Ser Asp
1 5 10